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=> s amphotericin and pure 7022 AMPHOTERICIN 422650 PURE L1

68 AMPHOTERICIN AND PURE

=> s l1 and chromatography 310553 CHROMATOGRAPHY L21 L1 AND CHROMATOGRAPHY

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ANSWER 1 OF 1 CA COPYRIGHT 2006 ACS on STN  $L_2$ 

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ΔR The invention discloses highly purified daptomycin and to pharmaceutical compns. comprising this compound The invention discloses a method of purifying daptomycin comprising the sequential steps of anion exchange chromatog., hydrophobic interaction chromatog. and anion exchange The invention also discloses a method of purifying daptomycin by modified buffer enhanced anion exchange chromatog. An improved method for producing daptomycin by fermentation of Streptomyces roseosporus is described. The invention also discloses HPLC methods for anal. of daptomycin purity. Methods of using lipopeptide micelles for purifying lipopeptide antibiotics, such as daptomycin, and using them therapeutically are disclosed. Thus, daptomycin was produced in a fermentation culture of S. roseosporus and partially purified daptomycin (9.9 Kg) was purified by microfiltration from 5500 L of fermentation broth. The partially purified daptomycin was further purified and resulted in a bulk daptomycin preparation with a purity of 91%. The daptomycin preparation contained 14 impurities as determined by HPLC anal. The daptomycin preparation was applied to a

Poros P150 anion exchange resin (PE Biosystems) in Tris buffer pH 7.0 containing 6M urea and allowed to bind to the resin. The resin was washed with 3 column vols. of buffer prior to initiation of a NaCl gradient in the same buffer. Alternatively, the contaminants can be effectively removed from the column with a fixed salt level of 30 mM NaCl. elution of purified daptomycin from the resin occurred at approx. 300 mM NaCl during a 0 to 1000 mM NaCl gradient. Daptomycin eluted from the column was greater than 99% pure as measured by the "first" HPLC

method. The purified daptomycin contained only one detectable daptomycin contaminant. Anhydrodaptomycin and B-isomer were undetectable (<0.01% contamination). The level of the unidentified contaminant was 0.1-0.5%.

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